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Incidence, Causes, and Outcomes of Out-of-Hospital Cardiac Arrest in Children

A Comprehensive, Prospective, Population-Based Study in the Netherlands

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Objectives This study sought to determine comprehensively the incidence of pediatric out-of-hospital cardiac arrest (OHCA) and its contribution to total pediatric mortality, the causes of pediatric OHCA, and the outcome of resuscitation of pediatric OHCA patients.

Background There is a paucity of complete studies on incidence, causes, and outcomes of pediatric OHCA.

Methods In this prospective, population-based study, OHCA victims younger than age 21 years in 1 province of the Netherlands were registered through both emergency medical services and coroners over a period of 4.3 years. Death certificate data on total pediatric mortality, survival status, and neurological outcome at hospital discharge also were obtained.

Results With a total mortality of 923 during the study period and 233 victims of OHCA (including 221 who died and 12 who survived), OHCA caused 24% (221 of 923) of total pediatric mortality. Natural causes of OHCA amounted to 115 (49%) cases, with cardiac causes being most prevalent (n = 90, 39%). The incidence of pediatric OHCA was 9.0 per 100,000 pediatric person-years (95% confidence interval: 7.8 to 10.3), whereas the incidence of pediatric OHCA from cardiac causes was 3.2 (95% confidence interval: 2.5 to 3.9). Of 51 resuscitated patients, 12 (24%) survived; among survivors, 10 (83%) had a neurologically intact outcome.

Conclusions Out-of-hospital cardiac arrest accounts for a significant proportion of pediatric mortality, and cardiac causes are the most prevalent causes of OHCA. The vast majority of OHCA survivors have a neurologically intact outcome. (J Am Coll Cardiol 2011;57:1822–8) © 2011 by the American College of Cardiology Foundation

There is a paucity of complete studies on incidence and causes of pediatric out-of-hospital cardiac arrest (OHCA) and on outcomes of cardiopulmonary resuscitation (CPR) of pediatric OHCA victims. Reported pediatric OHCA incidences range widely (from 6.0 to 19.7 per 100,000 pediatric person-years) (1–5), as do reported survival rates (from 0% to 19%) (1–8). The only 2 studies on neurological outcomes of pediatric OHCA reported a poor neurological outcome in less than half of those discharged from the hospital alive (1,6), and some researchers have even questioned whether CPR in children should be conducted at all, because neurological outcome and cost-effectiveness may be poor (5,9). Clearly, many questions have not been addressed fully. First, the large studies that aimed at identification of the incidence of pediatric OHCA included only OHCA

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cases in which emergency medical services (EMS) were involved (1,2), while excluding cases where EMS were not involved (coroners' cases), thereby underestimating the incidence of OHCA and confounding efforts at determining the proportion of OHCA in total pediatric mortality. Second, few studies reported the contribution of the single (groups of) causes of OHCA, and these studies included only OHCA cases where EMS were involved (1,4,6). Consequently, it is unclear which causes are the most prevalent in pediatric OHCA, although this information may have important implications in prevention programs.

We conducted a comprehensive, prospective, population-based study in the Netherlands using EMS and non-EMS sources to identify cases of pediatric OHCA to determine: 1) the incidence of pediatric OHCA and its contribution to total pediatric mortality; 2) the causes of pediatric OHCA; and 3) the outcome (overall and neurological) of CPR of pediatric OHCA victims.

Abbreviations and Acronyms

AED = automated external defibrillator
CPR = cardiopulmonary resuscitation
EMS = emergency medical services
ICD-10 = International Classification of Diseases-10th Revision
OHCA = out-of-hospital cardiac arrest
VF = ventricular fibrillation
VT = ventricular tachycardia

Methods

Setting. The investigation was a prospective population-based study of persons younger than 21 years who had OHCA between October 1, 2005, and February 1, 2010, in the North Holland province of the Netherlands. This study region covers 2,404 km^2 (urban and rural communities) and has a population of 2.4 million people, including 588,389 persons younger than 21 years (study population), of whom 28,069 were younger than 1 year (infants), 313,873 were 1 to 11 years of age (children), and 246,447 were 12 to 20 years of age (adolescents). We included all OHCA patients with whom EMS were involved (EMS cases), and those with whom coroners were involved (coroners' cases). The Medical Ethics Review Board of the Academic Medical Center, Amsterdam, approved the study and gave a waiver for the requirement of (written) informed consent.

EMS cases. The ARREST (Amsterdam Resuscitation Studies) were set up to establish the genetic and environmental determinants of OHCA in the general population (10) and the determinants of outcome of OHCA (11). Data from all OHCA cases with EMS involvement in 1 contiguous representative region of the Netherlands (the study region) are collected and stored in the ARREST database. In a medical emergency, people dial the national emergency number. When the EMS dispatcher suspects OHCA, he or she dispatches 2 ambulances (11), and a first responder (firefighters, policemen, general practitioner) equipped with an automated external defibrillator (AED). Ambulance personnel are equipped with a manual defibrillator and are qualified to perform advanced life support (12). After each CPR attempt, EMS paramedics routinely send the continuous electrocardiogram and impedance recordings from their manual defibrillators to the study center by modem (13). The ARREST study personnel, who visit the AED site shortly after OHCA, collect the AED electrocardiogram recording. The electrocardiograms are stored and analyzed with dedicated software (Code Stat Reviewer 7.0, Physio Control, Redmond, Washington). Rhythms are categorized as shockable (ventricular tachycardia [VT] and ventricular fibrillation [VF]) or nonshockable (asystole or electromechanical dissociation). Data items concerning the CPR procedure are collected according to the Utstein recommendations (14). All 4 EMS services in the study region participate in ARREST. The EMS cases were collected from the ARREST database.

Coroners' cases. When someone dies in the Netherlands, physicians are legally obliged to inspect the corpse and complete a death certificate. If the physician is unsure whether the patient died of natural causes, a coroner (physician) is contacted to inspect the corpse, determine the cause of death, and judge (in consultation with the public prosecutor) whether judicial autopsy is required. All reports on corpse inspections performed by the coroners are stored digitally at the Departments of Forensic Medicine of the Public Health Services. This database contains personal details and date and cause of death. In case of a natural cause of death, details on the circumstances and temporal course of the event also are available. Eighty percent of all coroners in the study region participated in this study. Coroners' cases were collected from this database.

Identification of OHCA cases. OHCA was defined as an out-of-hospital unexpected and abrupt loss of consciousness with loss of vital signs (pulse, blood pressure, respiration) and resulting in death or, if successfully resuscitated, survival to hospital discharge, or out-of-hospital unexpected death of someone seen in a stable medical condition fewer than 24 h previously (15). Perinatal sudden death and children known to have a terminal disease were excluded. During the study period, all patients in the ARREST database younger than 21 years of age were retrieved and reviewed manually and independently by 2 researchers (A.B. and J.B.). A patient was included if he or she: 1) was resuscitated, that is, underwent CPR by EMS personnel, a defibrillation attempt with an AED by a first responder or bystander (such defibrillation attempts were always followed by subsequent treatment by EMS), or both; or 2) was found dead by EMS personnel on arrival and fulfilled the OHCA definition. In case of discrepancy between the researchers, a specialized physician (H.L.T) arbitrated. Two researchers (C.v.d.W., Anneke Hendrix) reviewed all records in the coroners' database of persons younger than 21 years to assess whether the definition of OHCA was met. In case of discrepancy, a specialized physician (A.A.M.W.) arbitrated. All cases were

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checked for duplicates within the ARREST and coroners' databases.

Assessment of cardiac and noncardiac causes of OHCA. The included OHCA cases were classified based on the available medical information (by A.B., J.B., C.v.d.W) as cardiac or noncardiac. Out-of-hospital cardiac arrest was noncardiac when EMS rescuers, hospital physicians, or coroners identified a natural, noncardiac cause (e.g., asphyxia, intracranial hemorrhage) or nonnatural cause (e.g., traffic accident, drowning, suicide, violence); all other cases had a (presumed) cardiac cause and were considered cardiac OHCA (14,16).

Death certificate data. In addition to data from the ARREST database and the coroners' database, we also retrieved death certificate data from Statistics Netherlands, a Dutch governmental institution that collects age- and gender-specific statistics of all deaths in the Netherlands (national mandatory reporting system) (17). This allowed us to ascertain total pediatric mortality and to estimate the maximum number of potential OHCA cases. This served 2 purposes: 1) to establish the contribution of OHCA to total mortality in pediatric age groups; and 2) to gain insight into the completeness of our data collection. Statistics Netherlands records anonymous information on the site and causes of death as indicated on the death certificates; in case of nonnatural causes of death, information from the police and the public prosecutor also is used. The causes of death are classified according to the International Classification of Diseases-10th Revision (ICD-10). Deceased children in the ICD-10 diagnostic categories pregnancy, childbirth, and the puerperium (000-099), conditions originating in the perinatal period (P00-P96), and neoplasms (C00-D48) were excluded. Potential cardiac OHCA cases all were deaths in the ICD-10 categories that contained cardiovascular causes or unknown causes. Potential noncardiac OHCA cases were the remaining deaths in the ICD-10 categories that can occur suddenly (e.g., trauma, poisoning, drowning, suicide, and respiratory causes). We calculated the total number of potential cardiac OHCA cases by adding all out-of-hospital deaths in all ICD-10 categories that contained cardiovascular and unknown causes; to this, we added patients from the ARREST database who sustained cardiac OHCA, but eventually died in hospital, because these patients were not classified as out-of-hospital death by Statistics Netherlands. An analogous addition was used to calculate the total number of potential noncardiac OHCA cases.

Survival analysis. With the aim of establishing the outcome of CPR by EMS, we analyzed only OHCA that truly could be resuscitated cases by excluding OHCA victims who were found dead by EMS personnel on arrival, but in whom CPR still was initiated (e.g., for the parents' comfort). Survival status and neurological outcome at hospital discharge were obtained by contacting the hospital of admission. We estimated the cerebral performance category of each patient by reviewing the hospital charts: good cerebral performance, 1; moderate cerebral disability, 2; severe cerebral disability, 3; coma or vegetative state, 4; and death, 5 (18). A cerebral performance category score of 1 or 2 was classified as a neurologically intact outcome.

Statistical analyses. Descriptive statistics are reported as mean ± SD, median (25%, 75%), or number (percent) as indicated. Comparisons for continuous variables were made with an analysis of variance. Likelihood ratio chi-square analyses were used when discrete variables were compared across groups. The incidence rates were calculated per 100,000 pediatric person-years. The age category and sex-specific rates were calculated; these rates were adjusted by age and sex to the European Union population. All statistical tests were 2 tailed, and a p value of <0.05 was considered statistically significant. All statistics were performed using SPSS software version 16.0 for Mac (SPSS, Inc., Chicago, Illinois).

Results

Patient characteristics and incidence of OHCA. During the study period of 4 years and 4 months, 443 possible pediatric OHCA cases were identified. Of these, 210 did not meet the inclusion criteria because there was no loss of vital signs when EMS arrived (n = 142), the event occurred in the perinatal period (n = 56), or the event occurred in a patient with a terminal illness (n = 12). Thus, 233 persons fulfilled the definition of OHCA, including 221 who eventually died and 12 who survived. Of these 233 cases, 83 were EMS-only cases, 100 were coroners-only cases, and 50 were registered by both sources. With a total mortality of 923, the 221 OHCA victims who died amounted to 24% of total mortality in this age group. Fifty-two percent of all OHCA cases were adolescents, and 70% were males (Table 1). Most OHCA cases occurred at the place of residence (n = 111, 51%) or on the streets (n = 81, 38%). Ninety persons had cardiac OHCA. Among adolescents who had cardiac OHCA, 32% were engaged in exercise or sports at the time of OHCA. The adjusted incidence per 100,000 pediatric person-years of OHCA was 9.0 (95% confidence interval: 7.8 to 10.3), whereas that of cardiac OHCA was 3.2 (95% confidence interval: 2.5 to 3.9) (Table 2). The incidence of cardiac OHCA was highest among infants and similar among children and adolescents. According to the death certificate data, the total number of potential pediatric cardiac OHCA cases in the study period and study region was 103; of these, we registered 90 (87%) cases. The total number of potential pediatric noncardiac OHCA cases was 144, of which we registered 143 (99%).

Figure 1 shows the single causes of pediatric OHCA. Half of the 233 OHCA cases (n = 115, 49%) were the result of natural causes. Out-of-hospital cardiac arrest from cardiac causes was the most prevalent cause of OHCA (n = 90, 39%). Traffic accidents were the most prevalent cause among nonnatural causes (n = 60, 26%).

Table 1 Characteristics of Out-of-Hospital Cardiac Arrest From Cardiac and Noncardiac Causes

	All Causes (n = 233)	Cardiac Causes (n = 90)	Noncardiac Causes (n = 143)
Age, yrs	10.8 ± 7.7	7.4 ± 7.6	13.0 ± 7.0
<1 yr	45 (19)	35 (39)	10 (7)
1 to 11 yrs	66 (28)	25 (28)	41 (29)
12 to 20 yrs	122 (52)	30 (33)	92 (64)
Male	162 (70)	61 (68)	100 (70)
Ethnicity known	218 (94)	87 (97)	131 (92)
White	170 (78)	68 (78)	102 (78)
Arabic	17 (8)	3 (3)	14 (11)
Black	10 (5)	7 (8)	3 (2)
Turkish	11 (5)	5 (6)	6 (5)
Other	10 (5)	4 (5)	6 (5)
Site of OHCA known	216 (93)	89 (99)	127 (89)
Place of residence	111 (51)	67 (75)	44 (35)
On street	81 (38)	9 (10)	72 (57)
Public place	9 (4)	4 (4)	5 (4)
Sports or recreational facility	12 (6)	7 (8)	5 (4)
Other	3 (1)	2 (2)	1 (1)
Activity at the time of OHCA*			
Infants			
Activity known		29 (83)	
At rest		29 (100)	
During exercise/sport		0 (0)	
Children			
Activity known		17 (65)	
At rest		16 (94)	
During exercise/sport		1 (6)	
Adolescents			
Activity known		22 (76)	
At rest		15 (68)	
During exercise/sport		7 (32)	

Values are mean ± SD or n (%). *Only analyzed for OHCA from cardiac cause.
OHCA = out-of-hospital cardiac arrest.

Survival and neurological outcome of resuscitation of OHCA patients. The EMS were involved in 133 (57%) of the 233 pediatric OHCA patients. Of these patients, 73 OHCAs were the result of cardiac causes, including 4 that were witnessed by EMS personnel. Table 3 shows the characteristics of resuscitated patients. Infants were most likely to have OHCA at home (97% vs. 61% in children and 41% in adolescents, $p < 0.001$). An AED was used more frequently in adolescents (32% vs. 6% in children and 3% in infants, $p = 0.02$). Adolescents also had the highest percentage of shockable initial rhythm (82% vs. 33% in children and 3% in infants, $p < 0.001$). Although CPR was initiated in 69 OHCA victims, only 51 (14 infants, 17 children, 20 adolescents) truly could be resuscitated. The overall survival to hospital discharge of these 51 patients was 24% (12 of 51). The survival rates were not statistically significantly different between groups (29% [4 of 14] in infants, 12% [2 of 17] in children, 30% [6 of 20] in adolescents, $p = 0.37$). The overall proportion of neurologically intact outcomes among OHCA survivors was 83% (75% [3 of 4] in infants, 100% [2 of 2] in children, 83% [5 of 6] in adolescents).

Table 2 Incidences of Out-of-Hospital Cardiac Arrest From Cardiac and Noncardiac Causes

	All Causes (n = 233)	Cardiac Causes (n = 90)	Noncardiac Causes (n = 143)
Overall	9.0 (7.8–10.3)	3.2 (2.5–3.9)	5.8 (4.9–6.8)
Age <1 yr	33.8 (23.1–44.5)	25.8 (16.4–35.2)	8.0 (2.8–13.2)
Age 1 to 11 yrs	4.8 (3.6–6.0)	1.6 (0.9–2.3)	3.2 (2.2–4.2)
Age 12 to 20 yrs	11.7 (9.5–13.8)	2.7 (1.7–3.7)	9.0 (7.1–10.8)

Data are expressed as number per 100,000 pediatric person-years (95% confidence interval). All incidences are adjusted by age and sex to the European Union population.

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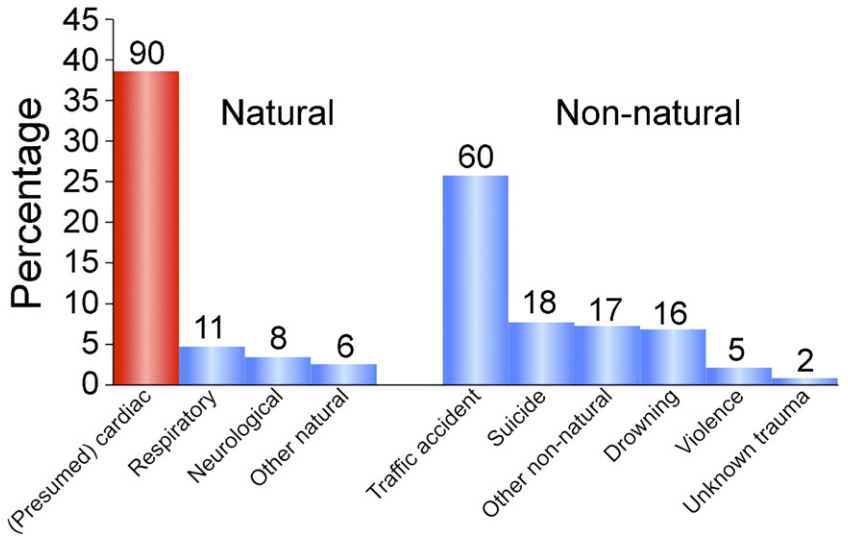

Figure 1 Causes of Out-of-Hospital Cardiac Arrest

The **left group of bars** represent natural causes, and the **right group of bars** represent nonnatural causes. All causes are shown as the percentage of the total number of out-of-hospital cardiac arrest cases. **Numbers above bars** indicate numbers of patients.

Discussion

Every year, 9 of 100,000 children in the Netherlands have OHCA. Cardiac causes account for 3 OHCA cases and noncardiac causes for 6 OHCA cases per 100,000 pediatric person-years. Cardiac causes are the most prevalent single cause of pediatric OHCA (39%), followed by traffic accidents (26%). The overall survival of resuscitated pediatric OHCA patients is 24%; the vast majority of survivors (83%) are discharged with neurologically intact function.

Comparison with other studies. Because different studies use various definitions for OHCA and include various age cutoffs, comparison of incidences between studies is difficult. We provide an overall incidence, an incidence for OHCA resulting from cardiac causes, and an incidence for OHCA from noncardiac causes, both unadjusted and adjusted for age and gender of the European Union population. Although our OHCA definition is comparable with that of the large population-based study by Kitamura et al. (1), we found somewhat higher incidences of total pediatric OHCA (9.0 vs. 8.0 per 100,000 pediatric person-years) and cardiac OHCA (3.2 vs. 2.3 per 100,000 pediatric person-years). It is conceivable that these differences are because we also included coroners' cases and studied a somewhat wider age range (subjects up to 20 years of age). We also found a higher OHCA incidence than 2 other recent population-based studies from the United States and Canada (2,3). These differences may be explained by disparities in definitions, because we included all causes of OHCA, whereas those studies excluded some nonnatural causes. Moreover, differences in socioeconomic and ethnic composition may be relevant (19,20). For example, the incidence of OHCA among adults in different states of the United States and Canadian sites ranges from 76 to 159 per 100,000 persons, compared with an incidence of 60 per 100,000 persons in the Netherlands (21,22). Finally, the proportion of OHCA among infants varies among populations and affects the overall incidence of pediatric OHCA. In our study, infants contributed 39% of all OHCA cases, comparable with other

Table 3 Operational Characteristics of Resuscitated Victims of Out-of-Hospital Cardiac Arrest From Cardiac Causes According to Age Group

	All (n = 69)	Age <1 yr (n = 29)	Age 1 to 11 yrs (n = 18)	Age 12 to 20 yrs (n = 22)	p Value
Witnessed collapse	41 (59)	11 (38)	14 (78)	16 (73)	0.03
Bystander CPR	52 (75)	19 (66)	14 (78)	19 (86)	0.53
Collapse at home	48 (70)	28 (97)	11 (61)	9 (41)	<0.001
AED connected	9 (13)	1 (3)	1 (6)	7 (32)	0.02
Time between emergency call and EMS arrival, min	12.1 (8.8–14.8)	12.2 (9.8–13.9)	11.1 (8.4–15.3)	12.0 (9.0–15.6)	0.99
Shockable initial rhythm	25 (36)	1 (3)	6 (33)	18 (82)	<0.001

Values are n (%) or median (25th to 75th percentile).
AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; EMS = emergency medical services.

studies (2,4,6). Chugh et al. (3) reported a higher proportion of infants (76%). The reason for this discrepancy is unknown, but sudden infant death syndrome is up to 5.7 times more prevalent in the United States than in the Netherlands (23). Biological differences and behavioral factors are thought to cause this disparity.

We report an overall percentage of 36% of VT and VF in our cases, and an even higher percentage in adolescents (82%). Other prospective studies reported a lower percentage of VT or VF, ranging from 3% to 9% (1–3,5–7), whereas 1 retrospective study reported an incidence of 19% (24). The presence of VT and VF as initial rhythm is correlated with a witnessed collapse, bystander CPR, use of an AED, and time to arrival of the ambulance (22). In comparison with other studies, patients in our study were more likely to have a witnessed collapse, receive bystander CPR, and be treated with an AED (1,3–7). Because VT and VF as initial rhythm has been associated with a better survival (25), one would expect a low survival among infants (VT and VF: 3%) and a high survival among adolescents (VT and VF: 82%). However, the survival to discharge did not support this expectation, being similar in infants and adolescents (29% and 30%, respectively). This apparent inconsistency between the low proportion of VT and VF and the relatively high survival rates also was observed in a large, prospective, observational study of in-hospital cardiac arrests in which the survival rates in children with VT and VF as an initial rhythm were comparable with those found in children with asystole (29% and 22%, respectively) (26).

In another study of 47 pediatric OHCA patients, 24 had bradycardia at presentation, and 12 of those survived to hospital discharge (27). Although other studies showed a poor neurological outcome after CPR (28), all but 2 survivors in our study were discharged with neurologically intact function. The outcomes observed in our study were better than those reported in 2 recent studies by Kitamura et al. (1) and Atkins et al. (2). Again, the higher rates of bystander CPR and bystander-witnessed collapse could have contributed to the better outcomes found in our study.

Resuscitation attempts in children are rare; of all OHCA patients in the ARREST registry in whom resuscitation was attempted, only 1.3% (51 of 3,922) were younger than 21 years. We observed a survival rate of 24% (12 of 51) among OHCA patients younger than 21 years, which was not different from that among adult OHCA patients in the ARREST registry (688 of 3,871, 17.9%, J. Berdowski, A. Bardai, M.T. Blom, H.L. Tan, R.W. Koster, unpublished data, October 2010).

Study strengths. A major strength of our study is that it was designed to establish the incidence, determinants, and outcomes of OHCA in the general population, allowing comprehensive and accurate data collection of all cases from the site of cardiac arrest until discharge from the hospital, including neurological outcome in OHCA survivors. Our study is the first study that aims to establish the contribution of OHCA to total pediatric mortality. Estimation of the incidence of OHCA within a particular region can be hampered by the fact that individuals who reside outside of this region may experience OHCA in the study region and vice versa. In a pediatric population, this confounder is probably less important, because children travel less (far) than adults. Only 7% of children in this study resided outside the study region. Other studies on the incidence of OHCA do not comment on this potential confounder.

Study limitations. Because only a national mandatory reporting system for OHCA, not present in the Netherlands, would ensure capture of all OHCA cases, we might have missed some cases. The incidences that we reported for OHCA that are based on EMS and coroners' databases thus may underestimate the true OHCA incidence, in particular because not all coroners in the study region contributed to the study. Yet, by analyzing data from a national mandatory reporting system for all mortality in the Netherlands (Statistics Netherlands), we verified that the number of cases that we might have missed was relatively small. We identified 90 cardiac OHCA cases, including 7 cardiac OHCA cases that survived to hospital discharge, whereas Statistics Netherlands reported 92 potential cardiac OHCA cases (excluding surviving OHCA victims). Similarly, we found 143 noncardiac OHCA cases, whereas Statistics Netherlands reported 137 potential noncardiac OHCA cases (excluding surviving OHCA victims). These findings indicate that our reported incidences are close to the actual incidences.

Second, the cause of OHCA was considered cardiac when evidence for a noncardiac or non-natural cause was absent, as recommended (14,16) and reported (1,2) by others. Because this cardiac category is a diagnosis by exclusion, this may lead to an overestimation of the proportion of cases that were considered to be the result of cardiac causes. This definition may particularly be problematic in case of OHCA in infants (sudden infant death syndrome). Only 33% of infant OHCA cases were alive when EMS arrived, allowing a diagnostic workup, whereas autopsy data were absent in virtually all cases (autopsy is not mandatory in the Netherlands). Thus, the cause of OHCA was unknown in most infants and was classified as cardiac, according to our definition (1,2,13,14). Yet, sudden infant death syndrome is believed to result often from respiratory causes (23,29).

Conclusions

In this prospective, population-based study, we established that OHCA accounts for 24% of total pediatric mortality and that cardiac causes are the most prevalent causes of OHCA. The vast majority of survivors of pediatric OHCA have a neurologically intact outcome.

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